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10/660,202	09/11/2003	Orn Almarsson	TPI-350C1	6536

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EXAMINER	
CLAYTOR, DEIRDRE RENEE	
ART UNIT	**PAPER NUMBER**
1617	

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12/10/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/660,202	ALMARSSON ET AL.	
	Examiner	Art Unit	
	Renee Claytor	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 October 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,9-11 and 38-42* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,9-11 and 38-42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response filed on 10/1/2007 is hereby acknowledged. Currently, claims 1-2, 9-11 and 38-42 are pending, with claims 3-8 and 12-37 being cancelled.

Response to Arguments

Applicants argue over the 35 USC 112, first paragraph rejection (Written Description) that a *prima facie* case providing reasons why one skilled in the art would not have recognized that the inventor was in possession of the claimed invention has not been established and that the rejection fails to establish a prima facie case that the written description provided is insufficient.

In response to the above arguments, it is noted that claim 1 broadly reads on any solid API and any co-crystal former that is liquid or solid, and where the components are hydrogen bonded to one another, or the co-crystals with any of the numerous diverse and different co-crystal formers in claim 2 or APIs as in claim 9. There is no description to convey to one of skill in the art that the inventors were in possession of the numerous and diverse co-crystals as claimed, including any API and any co-crystal former that are hydrogen bonded and are solid or liquid. Therefore, the rejection is maintained.

Applicants argue over the 35 USC 112, first paragraph rejection (Enablement) that the specification sets forth substances that are co-crystal formers as well as APIs and clearly provides teaching of the starting materials suitable for use in the claimed invention. Applicants further argue that the specification sets forth at least one high throughput method for the preparation of co-crystals. Applicants conclude by stating

that there are known methods for high throughput development of novel crystalline forms of known APIs.

In response to the above arguments, it is noted that the specification is enabled for the preparation and use of the particular pharmaceutical co-crystals as recited in claim 11; however, the specification is not enabled for the preparation of all co-crystals having any API that is solid, as broadly recited in claim 1. As discussed in the rejection, the state of the art regarding the formation of different crystalline forms is unpredictable due to the numerous different crystallization factors needed to be controlled to provide different crystal states. Further, the formation of crystals is usually arrived at via experimentation. The scope of claim 1 is very broad and reads on any API that is solid with any crystal co-former that is solid or liquid and where the components are hydrogen bonded. As explained previously, the specification does not provide any direction or guidance as to how to go about manufacturing all of the different crystal forms that contain an API and a co-crystal former that are hydrogen bonded to one another. Accordingly, the rejection is being maintained.

Applicant's amendments and arguments have necessitated the withdrawal of the 35 USC 102 rejections over Oswald et al., Remenar et al., Fleishman et al., Zaworotko et al., Dvorkin et al., Almarsson et al., and Childs et al. In particular, Applicants point out the priority documents that were filed before the publication dates of Oswald et al, Remenar et al., Fleishman et al. and Zaworotko et al. and Applicants have deleted subject matter that was contained in Dvorkin et al., Almarsson et al. and Childs et al.

Regarding the Double Patenting rejections, it is noted that Applicants amendments have necessitated the removal of the obviousness-type double patenting rejection over Remenar et al. (US Patent 7,078,526); however, the obviousness-type double patenting rejections over Applications 10/546,963, 10/570,405, 10/551,014, and 10/926,842 remain obvious over the pending claims and are given below.

Due to Applicants amendments to the claims, the following modified rejections are given below.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Written Description Rejection

Claims 1-2, 9-10 and 38-42 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

In particular, Applicants have only shown the formation of the particular co-crystals recited in claim 11, such as for example crystals of cabamazepine and saccharin, but do not exemplify or otherwise show the formation of all co-crystals containing any solid API and any co-crystal former that is liquid or solid, and where the components are hydrogen bonded to one another, or co-crystals with any of the numerous and divers different co-crystal formers in claim 2 or APIs as in claim 9. Applicants have not described or shown how the numerous and diverse different co-crystals as claimed could be obtained.

The specification only describes the preparation of the particular co-crystals recited in claim 11 (see pages 7-10, in particular.) Accordingly, the specification does not describe the claimed subject matter in a manner sufficient to convey to one of ordinary skill in art that the inventors were in possession of the entire invention, including the formation of co-crystals containing any API and any co-crystal former that are hydrogen bonded and are solid or liquid, as recited in the claims.

Enablement Rejection

Claims 1-2, 9-10 and 38-42 are rejected under 35 U.S.C. 112, first paragraph, for lacking enablement for the full scope of the claims. The specification is enabling for the preparation and use of the particular pharmaceutical co-crystals as recited in claim 11, such as co-crystals of carbamazepine and saccharin, or celecoxib and nicotinamide.

However, the specification is not enabling for the preparation of all co-crystals having any API that is solid, and any co-crystal former that solid and liquid, where the components are hydrogen bonded to one another, as recited in claim 1, or all co-crystals having the numerous and diverse APIs and co-crystal formers as in claims 2, 9-10 and 38-42.

The instant specification fails to provide information that would allow the skilled artisan to fully make and use the instant invention without ***undue experimentation***. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set fourth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

(1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

1. The nature of the invention: The instant invention pertains a co-crystal composition containing a solid API and a solid or liquid co-crystal former, where the API and co-crystal former are hydrogen bonded to one another.

2. The state of the prior art: The skilled artisan would view the formation of different crystalline forms as being unpredictable due to the numerous different crystallization factors needing to be controlled to provide different crystal states, as well as the unpredictability in predicting the different types of crystals that may exist. For example, as disclosed by Angelo Gavezzotti ("Are Crystal Structures Predictable?" by Gavezzotti, Acc. Chem. Res, 1994, Vol. 27, pages 309-314), the formation and structure of crystals are unpredictable at best (see first full paragraph, in particular.) Gavezzotti teaches that it can be unpredictable whether compounds will crystallize at all, crystal growth from solution is known to be problematic, and in general "a crystal is more readily destroyed than built" (see first full paragraph of right hand column on page 309.) Thus, Gavezzotti teaches that the production of crystals is unpredictable at best, with the particular process parameters suitable for crystallizing a compound typically not being known in advance, and thus desired crystals can generally only be arrived at via experimentation and dealing with "tough problems in the control of solidification, crystal growth, and crystal morphology, mainly due to perverse kinetic control of nucleation (see first full paragraph of right hand column on page 309.)

3. The relative skill of those in the art: the relative skill of those in the art is typically very high, i.e. experienced scientists having advanced degrees in the chemical and biochemical fields.

4. The predictability of the art: As discussed above, the production of crystal forms is highly unpredictable, with crystal growth from solution being problematic. (see page 309 of Gavezzotti, in particular.)

5. The breadth of the claims: the unpredictable nature of the invention is exacerbated by the breadth of the claims. The claims require co-crystal composition that has any API that is solid, in general, with any crystal co-former that is solid or liquid, in general, where the components are hydrogen bonded, as in claim 1. Thus, the claims as instantly presented encompass all co-crystals having any solid API and any solid or liquid co-crystal former, where the components are hydrogen bonded to one another.

6. The amount of direction or guidance presented: the specification does not provide any direction or guidance as to how to go about manufacturing and/or finding all of the different crystal forms that contain an API and a co-crystal former and that are hydrogen bonded to one another, and that thus fall within the scope of the claim. The specification generally teaches that hydrogen bonding is a dominant interaction in the formation of a co-crystal (see page 10 of specification, in particular), but does not teach how one of ordinary skill in the art would go about finding the proper crystallization process parameters, such as the proper crystallization solvent, temperature, etc, to

allow for the formation of all of the co-crystals encompassed by the claims, without requiring undue experimentation.

7. The presence or absence of working examples: The specification does not provide working examples that are sufficient to show one of ordinary skill in the art how to arrive at all of the co-crystal forms. Instead, the specification merely provides examples showing the fabrication of the particular co-crystals recited in claim 11, including carbamazepine and saccharin, and topiramate and 18-crown-6 co-crystals (see Examples 1-37, in particular.) Thus, while the specification provides guidance for forming the particular co-crystals specifically disclosed in the specification and recited in claim 11, the specification does not provide adequate guidance as to how one of ordinary skill in the art could prepare all other crystals containing any API and co-crystal former.

8. The quantity of experimentation necessary: As the specification does not provide adequate guidance to allow one of ordinary skill in the art to readily determine the manufacturing conditions required to achieve crystallization of all of API/co-crystal formers, nor to determine which combinations of API and co-crystal former would even be capable of being recovered in crystal form, it is considered that one of ordinary skill in the art would have to engage in **undue experimentation** in order to be able to fully make and use the invention to the full extent of the claims.

In particular, as the parameters crucial to forming all of the API/co-crystal former crystals are not known, one of ordinary skill in the art would have to perform an exhaustive search to find all of those APIs and co-crystal formers, as well as all crystallization parameters, that are necessary to provide the crystal forms. To make all of the possible crystals, one of ordinary skill in the art would have to first have to select a particular API and co-crystal former combination, and then discover the means of achieving the crystalline form of the combination by performing numerous and exhaustive crystal manufacturing processes and making incremental changes in each manufacturing parameter, such as solvent and temperature parameters, to try and obtain the compounds in co-crystal form. If the components failed to crystallize, the crystal manufacturing process would have to be repeated, again with incremental changes in parameters, to attempt to achieve a new crystal form. If a crystal were achieved, the crystal would have to be analyzed by X-ray diffraction or other method to determine whether hydrogen bonding existed in the crystal. The above procedure would have to be repeated numerous different times with a variety of different process parameters, as well as with different APIs and co-crystal formers, in order for one of ordinary skill in the art to discover all those co-crystal forms that fall within the scope of the claim, and thus to be able to fully make and use the invention commensurate with the full scope of the claim. Therefore, the skilled artisan would have to exercise **undue experimentation** to practice the instant invention.

Thus, the specification fails to provide sufficient support for the broad recitation of a co-crystal composition containing any solid API, in general, with any solid or liquid co-crystal-former, in general, in which the components are hydrogen bonded to each other. As a result, one of ordinary skill in the art would be required to perform an exhaustive search for the embodiments of the co-crystal compositions that are suitable for the practice of the invention.

Genentech, 108 F.3d at 1366, states that "a patent is not a hunting license. It is not a reward for a search, but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable."

Therefore, in view of the *Wands* factors and *In re Fisher* (CCPA 1970) discussed above, to practice the claimed invention herein, a person of ordinary skill in the art would have to engage in *undue experimentation* to make and use all of the co-crystal compositions encompassed by the instant claims, with no assurance of success.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims

are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-2, 9-11 and 38-42 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-10 of U.S. Patent No.7,078,526 to Remenar et al. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are to co-crystals of APIs and co-crystal formers, including the specific crystals listed in claim 11, such as itraconazole and tartaric acid, whereas the patented claims are to only the specific co-crystal that contains itraconazole and tartaric acid. Accordingly, the instant claims are obvious over the specific patented co-crystal, and thus are not patentably distinct over the 7,078,526 patent.

Claims 1-2 and 10 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 86-93 of copending Application No. 10/546,963, as published in U.S. Patent Application

Publication No. 2007/0059356 to Almarsson et al. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are to co-crystals having any API and any co-crystal former that are hydrogen bonded, whereas the published claims are to co-crystal compositions having APIs and co-crystal formers with functional groups that allow for hydrogen bonding. Accordingly, the broader class of co-crystals as claimed is obvious over the co-crystals having the specific functional groups as in the published application, and the instant claims are not patentably distinct from those in the 2007/0059356 publication.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1-2, 9-11 and 38-42 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-49 and 72-87 of copending Application No. 10/570,405, as published in U.S. Patent Application Publication No. 2007/0021510 to Hickey et al. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are to co-crystals having any API and any co-crystal former that are hydrogen bonded, including modafinil and malonic acid, whereas the published claims are to co-crystal compositions having modafinil as the APIs and co-crystal formers that hydrogen bond to one another, such as malonic acid. Accordingly, the broader class of co-crystals as claimed is obvious over the specific modafinil co-crystals as in the

published application, and the instant claims are not patentably distinct from those in the 2007/0021510 publication.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1-2, 9-11 and 38-42 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 66-72 of copending Application No. 10/551,014, as published in U.S. Patent Application Publication No. 2006/0223794 to Bourghol Hickey et al. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are to co-crystals having any API and any co-crystal former that are hydrogen bonded, including olanzapine and nicotinamide, whereas the published claims are to the specific co-crystal compositions having olanzapine and nicotinamide as the co-crystal components. Accordingly, the broader class of co-crystals as claimed is obvious over the specific olanzapine co-crystals as in the published application, and the instant claims are not patentably distinct from those in the 2006/00223794 publication.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1-2, 9-11 and 38-42 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 2-7, 16 and 18 of copending Application No. 10/926,842, as published in U.S. Patent Application Publication No. 2005/0070551 to Remenar et al. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are to co-crystals having any API and any co-crystal former that are hydrogen bonded, including itraconazole and various acids such as succinic acid, fumaric acid and tartaric acid, whereas the published claims are to the specific co-crystal compositions having itraconazole and acids such as malonic acid, fumaric acid, tartaric acid, etc, as well as other co-crystal forms. Accordingly, the scope of the instant claims overlaps with that of the published application, and accordingly, the instant claims are not patentably distinct from those in the 2005/0070551 publication.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

Claims 1-2, 9-11 and 38-42 are free of the art. The Examiner suggests to the Applicant to consider:

1. deleting part c) from claim 1, adding the limitation to claim 9 into part c),
2. delete claim 2,

3. keep claims 10-11 and 38-42.

The Examiner feels that the above changes will put the application in better condition for allowance.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Renee Claytor whose telephone number is 571-272-8394. The examiner can normally be reached on M-F 8:00-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Renee Claytor